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Assessment of Serum level of Zinc alpha glycoprotein in patients with acne vulgaris

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Abstract

In the context of acne vulgaris (AV), which is a prevalent, long-term skin illness, the pilosebaceous units of the skin may become blocked or inflamed, resulting in both inflammatory and noninflammatory lesions, as well as a combination of both. Even the back and chest might be affected by this disease. Acne is one of the most common skin problems among teens, accounting for more than 85% of the population. P. acnes, seborrhea, sebaceous gland hyperplasia, and follicular hyper keratinization all play a role in the pathogenesis of an acne lesion. An increased chance of developing type 2 diabetes, cardiovascular disease (CVD), weight gain, and other health issues is associated with the metabolic syndrome (MetS) or syndrome X. Serum zinc alpha glycoprotein, BMI, and the severity of acne will be examined in this research to see whether there is a correlation. According to the worldwide acne grading system, this research comprised 40 instances of moderate to severe acne vulgaris and 40 healthy control subjects. They were chosen among patients at the Benha University Hospital Dermatology and Andrology Department's Outpatient Clinic. The trial lasted anywhere from six to twelve months. In terms of age, gender, and location, there was no statistically significant difference in any of the three groups tested. P=0.001 showed that cases had a higher mean BMI than controls. As compared to the control group, there was a statistically significant difference (p=0.044). Only 17.5 percent of acne sufferers had mold-related acne, which had a mean age of onset of 13.5 years. In ZAG, there was a statistically significant difference between the two groups tested. ZAG has a negative association with BMI, acne duration, and severity, according to the results of this study. ZAG was shown to have a statistically significant relationship with the severity of acne in the patients who were investigated. Severe cases exhibited lower ZAG than mild and moderate ones.

Key words: Zinc alpha glycoprotein, Serum, acne vulgaris.

1. Introduction

Acne vulgaris is a common, long-term skin condition that arises when hair follicles and their surrounding sebaceous glands become blocked or inflamed. Non-inflammatory lesions, inflammatory lesions, or a combination of both may be seen on the face, back, and chest [1].

This illness affects roughly 85 percent of young people between the ages of 12 and 25 globally, and it is currently the most prevalent skin problem among late teens.

An growing number of people in low- and middle-income nations are becoming obese. The development of severe acne may be linked to obesity, which has been linked to a rise in peripheral androgen levels [3].

Body mass index (BMI) is a reliable way of determining obesity. Exercise and body mass index have been overlooked in acne causation. However, in developing nations, the level of physical activity among teenagers is decreasing, leading to a rise in obesity among adolescents. Because of this, acne may be on the increase among adolescents in this age bracket [4].

After being precipitated by zinc salts in 1961, adipokine zinc-2-glycoprotein (ZAG) was initially isolated as a single-chain polypeptide and recognised as an adipokine. ZAG has been shown to improve lipid and glucose metabolism, as well as modulate insulin sensitivity, and hence improve insulin sensitivity. The pathophysiology of cancer cachexia has also been linked to the presence of this biomarker in certain patients [5].

Several studies have shown that ZAG has a role in controlling body weight and promoting lipolysis in adipocytes, and ZAG deficiency has been linked to the skin's barrier function [6].

Serum zinc alpha glycoprotein, BMI, and the severity of acne will be examined in this research to see whether there is a correlation.

2. Patients and Methods

Studypopulation

This study was conducted on 30 patients with moderate to severe acne vulgaris for at least one-year duration presented to Dermatology outpatient clinic at Benha university hospital, from January…..to November….

Studydesign

The present study was a Case-control study toinvestigate serum zinc alpha glycoprotein in patients with acne vulgaris and the possible relationship between serum zinc alpha glycoprotein, BMI and severity of acne .The subjects were randomly divided into two groups(40 patients each):

- **GroupI:15**cases complaining of moderate to severe acnevulgaris according to global acne grading (GAGs) [7]
- **GroupII:15** matched healthy controls controls matched to cases as regards socio-demographic characteristics and not complaining of acne

Ethical considerations

This study was approved by the local ethical committee. Informedconsent for treatment and scalp

biopsy was obtained from every patientprior toanyprocedure.

Inclusioncriteria
- Age ≥18 years.
- Patients with moderate to severe acne vulgaris. Global acne grading [7]

Exclusioncriteria
- Any participant with any other dermatological conditions or any psychiatric disorders
- History of any systemic diseases eg.: liver diseases, diabetes mellitus hyperlipidemia or hypertension .
- History of drug intake

Allpatientsweresubjectedto

1-Detailedhistory taking:
- Onset, course and duration of the disease.
- History of any systemic diseases eg. : liver diseases , diabetes mellitus hyperlipidemia or hypertension .
- History of drug intake
- History of chronic disease, malignancy, infection, autoimmune disease, liver or renal disease

2-Clinicalexamination:
- General examination to exclude presence of any co-morbidities
- Weight in kilograms.
- Height in centimeters.
- Body Mass Index(BMI).

$$= \frac{\text{Weight in Kg}}{(\text{Height in meters})^2}$$

- Local Examination: All patients had been subjected to assess site, distribution and severity of acne according to GAG score.

Evaluate degree of acne severity based on the global acne grading system (GAG score):
- Methods of measuring the severity of acne vulgaris include simple grading based on clinical examination, lesion counting, and those that require complicated instruments such as photography, fluorescent photography, polarized light photography, video microscopy and measurement of sebum production. The two commonly used measures are grading and lesion counting Table (1).

Table (1) Comparison between grading and lesion counting

Grading	Lesion counting
Involves observing the dominant Lesions,and estimating the extent of involvement	Involves recording the number of each type of acne lesion and determining the overall severity
Subjective method	Objective method
Simple and quick method	Time consuming method
Less accurate	More accurate
Does not distinguish small differences in therapeutic response	distinguishes small differences in therapeutic response
Effect of treatment on individual lesions cannot be estimated	Effect of treatment on individual lesions can be estimated
Used in offices and clinical settings	Used in clinical trials

Serum zinc alpha glycoprotein was measured
- Five ml of fasting blood samples were collected by standard venipuncture into evacuated tubes with and without EDTA.
- All samples were kept at room temperature for at least 60 min to allow the blood clot formation and were later centrifuged at 3000 RPM for 10 min.
- Plasma and serum were stored at −80 °C until analysis.

Serum zinc alpha glycoprotein was measured by enzyme-linked immunosorbent assay (ELISA) according to manufacture instructions.

Statistical analysis

Statistical analysis was done using SPSS software version 27 (IBM, 2020). Graphical and tabular presentation was done. Quantitative variables were summarized as mean, median, range and standard deviation. Qualitative variables were presented as frequencies and proportions. Shapiro-Wilk test was used to determine the distribution characteristics of variables and variance homogeneity.

3. Results

Demographic data is presented in table (1) that shows that there was no statistically significant difference between that studied groups in age, gender and residence. Cases had significantly higher mean of BMI than controls (p=0.003).

Table (2) Grades of obesity of the studied patients

		Case group (n=40)	Control group (n=40)	Test of sign.	P
Normal	**Count**	19	28		
	% within Group	47.5%	70.0%		
Over weight	**Count**	15	7		
	% within Group	37.5%	17.5%	6.742	0.044
Obese	**Count**	6	5		S
	% within Group	15.0%	12.5%		

Table (2) shows cases had significantly higher overweight and obese patients than controls (p=0.044).

Table (3) Relation between ZAG and sex of the studied patients

ZAG	Sex		Test of sig.	P
	Males	**Females**		
Mean ± SD	25.3 ± 17.0	27.8 ± 21.3	MW	
Median	17.8	19.4	0.1	0.9
Range	7.4 – 53.9	8.1 – 86.0		

MW; man Whitney test.

Table (3) shows that there was no statistically significant relation between ZAG and sex of the studied patients.

Table (4) Relation between ZAG and residence of the studied patients

ZAG	Residence		Test of sig.	P
	Urban	Rural		
Mean ± SD	29.8 ± 22.2	24.3 ± 18.3	MW	
Median	24.6	17.8	0.9	0.4
Range	8.1 – 86.0	7.4 – 72.4		

MW; man Whitney test.

Table (4) shows that there was no statistically significant relation between ZAG and residence of the studied patients.

4. Discussion

Statistically, there was no statistically significant difference in demographic features between the two groups tested.

For their case-control research, [8] recruited 50 patients with acne vulgaris (cases) and 50 age- and sex-matched controls without acne. Cases and controls were not statistically different in terms of age, BMI, or sexual distribution.

When it comes to overall age and BMI,[9], found statistically significant differences between the two groups, with the mean age of 32.2 5.2 years and 36.4 7.0 years, respectively, and the BMI of 22.5 3.9 kg/m2.

According to previous studies, women are more likely to get acne than men [10]. Also in 2010, researchers from The World Health Organization found that just 8.96 percent of men worldwide had acne, compared to a female prevalence of 9.81 percent [11]. The earlier beginning of puberty in girls compared to boys, as highlighted (2), may explain the increased incidence of acne in females at younger ages.

Acne was more prevalent in girls (75 percent) than men (25 percent) in a research [12], with a p value of 0.04 attributable to the larger number of females, hereditary and hormonal causes. Another research in Egypt's Ismailia city found that the prevalence of acne was higher among women (56 percent) than men (44 percent) [13]. In contrast, a Chinese community-based research on teenagers and adults found that men had a greater incidence of acne than girls between the ages of 18 and 20 years old (10.4 percent) [14].

acne is more common in overweight and obese persons (BMI 23 kg/m2 or BMI 25 kg/m2) than in underweight individuals (BMI 18.5 kg/m2) or those of normal weight (17.5 kilogrammes per square metres to 23 kilogrammes per square metres). In order to determine the link between BMI and acne risk, a pooled odds ratio was constructed. Using a 95 percent confidence interval of 1.97–2.83, the OR of 2.36 (overweight/obese BMI vs normal/underweight BMI) indicates that BMI has a substantial impact on how acne is presented. Because the case-control research [16] was eliminated because of study design, their findings were consistent with those of the cross-sectional studies that were analysed. People who are obese or overweight are more likely to have high glycemic loads, which may lead to an increase in sebum production, which can lead to the development of acne lesions. BMI and acne may be influenced by dietary variables [17].

Acne development occurred at a median age of 13.5 years; 42.5 percent had severe acne, and only

17.5 percent had moderate acne, according to the results of this research.

[18] observed that there were 20 instances of moderate illness severity (50%) and 20 cases of severe disease severity (50%) in their investigation (50 percent).

While 84% of the patients investigated [19] had mild illness severity, just 16% had intermediate disease severity.

There were 65.5 percent of patients who were considered normal in terms of BMI, with 12 percent classified as overweight; 20.5 percent as underweight; and 2 percent as obese. The majority of individuals were suffering from acne of a moderate to severe severity (52.6 percent). Only 4.8 percent of those polled experienced acne of this severity. In women, acne of grades 2 and 3 was more frequent, whereas in men, acne of grades 3 and 4 was more common. 48 (19.3%) of the patients had a family history of acne. The mean BMI was within the normal range for all grades of acne when compared to BMI. Grade 4 acne was seen in the majority of very obese patients, whereas the majority of severely overweight patients had acne of grade 2, and the majority of severely underweight patients had acne of grade 1. However, there was no correlation between BMI and acne grades (p=0.129). In the same way, there was no correlation between age and acne severity (p=0.61)

Since we are investigating serum zinc alpha glycoprotein levels in acne patients, this is a first-of-its-kind research looking at the link between serum zinc alpha glycoprotein, body mass index (BMI), and acne severity.

ZAG was shown to have a statistically significant difference between the two groups of people evaluated in our research. ZAG had statistically significant negative connections with BMI, the length and severity of acne, and ZAG was also negatively correlated with acne severity. ZAG was shown to have a statistically significant relationship with the severity of acne in the patients who were investigated. Severe cases exhibited lower ZAG than mild and moderate ones.

The findings of Yeung et al., (20), who studied the connection between blood ZAG levels and obesity and cardiometabolic risk factors in people, were in agreement with our findings. Men had significantly greater levels of serum ZAG (P 0.001 vs. women), the researchers discovered. Fasting insulin and insulin resistance indices were positively associated with serum ZAG (all P 0.005, adjusted for age and gender), while high-density lipoprotein cholesterol was negatively associated (P = 0.008, adjusted for age and gender). Serum ZAG was also positively associated with waist circumference and BMI, as well as fasting insulin and insulin resistance indexes, as well as diastolic blood pressure and serum triglycerides. The metabolic syndrome was associated with a steadily rising level of this marker (P for trend 0.001). Male gender, metabolic syndrome (or type 2 diabetes and serum triglycerides) and C-reactive protein were all shown to be significantly linked with serum ZAG in multivariate analyses (all P 0.002).

There have been many investigations done to see whether there is a connection between ZAG and other skin conditions. ZAG, a keratinocyte-derived factor, has been shown to regulate melanocyte proliferation and densification. It may also be used as an indicator of cell maturation and differentiation. Vitiligo is characterised by a deficiency of ZAG, which is predicted to restrict melanocyte proliferation, and if Langerhans cells are considered poorly differentiated melanocytes, this impairment in the maturation or differentiation of melanocytes may be linked to ZAG deficiency (21).

In vitiligo therapy, Bagherani et al. (22) hypothesised that zinc would be helpful. Zinc has been demonstrated in several experiments to precipitate ZAG (23).

In normal keratinocytes, IFN-g increases ZAG expression 11-fold, but in psoriatic keratinocytes, it substantially decreases it. This was discovered in the research by CHEN et al. (24).

Premature coronary artery disease (PCAD) is associated with a high level of serum ZAG, which has been linked to a variety of conventional risk factors, such as obesity, type 2 diabetes, high blood pressure, dyslipidemia, renal disease, polycystic ovarian syndrome, and smoking. Research by Qu and colleagues (26) suggested that serum ZAG might serve as a novel biomarker for insulin resistance and metabolic syndrome.

When compared to the controls, ZAG levels in the PCAD and NPCAD groups (without premature coronary artery disease) were considerably lower in the PCAD group (8.03) and ZAG levels in the NPCAD group (8.08), respectively. According to the receiver operating curve (ROC) analysis, serum ZAG had poor diagnostic performance for PCAD (AUC = 0.659, 95% CI 0.612–0.705, p 0.05). The sensitivity and specificity for distinguishing PCAD patients from controls were 50.5 and 78.0 percent, respectively, at the threshold value of 7.955 g/mL serum ZAG. Clinical variables such as age, gender, BMI and SBP were combined with ZAG to increase the diagnostic accuracy by 82.6 percent and 95.0 percent respectively. The AUC was 0.9557 (95 percent confidence interval, 0.940-0.975), which is significantly better than the 0.940–0.975 (95 percent confidence interval, 0.940-0.975) AUC for ZAG alone.

5. Conclusion

There was statistically significant difference between that studied groups in ZAG. Cases had significantly lower mean of ZAG than controls ($p<0.001$).. There were statistically significant negative correlations between ZAG and BMI,

duration and severity of acne. There was a statistically significant relation between ZAG and severity of acne in the studied patients. Severe cases had significantly lower ZAG compared to mild and moderate cases.

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